Mitochondrial Transfer by Photothermal Nanoblade Restores Metabolite Profile in Mammalian Cells.

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Public Summary:
Mitochondrial DNA (mtDNA) sequence alterations are challenging to generate but desirable for basic studies and potential correction of mtDNA diseases. Here, we report a new method for transferring isolated mitochondria into somatic mammalian cells using a photothermal nanoblade, which bypasses endocytosis and cell fusion. The nanoblade rescued the pyrimidine auxotroph phenotype and respiration of rho0 cells that lack mtDNA. Three stable isogenic nanoblade-rescued clones grown in uridine-free medium showed distinct bioenergetics profiles. Rescue lines 1 and 3 reestablished nucleus-encoded anapleurotic and catapleurotic enzyme gene expression patterns and had metabolite profiles similar to the parent cells from which the rho0 recipient cells were derived. By contrast, rescue line 2 retained a rho0 cell metabolic phenotype despite growth in uridine-free selection. The known influence of metabolite levels on cellular processes, including epigenome modifications and gene expression, suggests metabolite profiling can help assess the quality and function of mtDNA-modified cells. Thus, this apparatus allows the transfer of mitochondria from a host cell to a recipient cell, bypassing the typical and tedious approach of cell fusion assays.

Scientific Abstract:
mtDNA sequence alterations are challenging to generate but desirable for basic studies and potential correction of mtDNA diseases. Here, we report a new method for transferring isolated mitochondria into somatic mammalian cells using a photothermal nanoblade, which bypasses endocytosis and cell fusion. The nanoblade rescued the pyrimidine auxotroph phenotype and respiration of rho0 cells that lack mtDNA. Three stable isogenic nanoblade-rescued clones grown in uridine-free medium showed distinct bioenergetics profiles. Rescue lines 1 and 3 reestablished nucleus-encoded anapleurotic and catapleurotic enzyme gene expression patterns and had metabolite profiles similar to the parent cells from which the rho0 recipient cells were derived. By contrast, rescue line 2 retained a rho0 cell metabolic phenotype despite growth in uridine-free selection. The known influence of metabolite levels on cellular processes, including epigenome modifications and gene expression, suggests metabolite profiling can help assess the quality and function of mtDNA-modified cells.